Summaries

of the manuscripts of Chief Assist. Prof. Metodi Georgiev Traykov, PhD for participation in a competition for the academic position "Associate Professor" of the area of higher education: 4. Natural Science, Mathematics and Computer Science in professional field 4.6. Informatics and Computer Science announced in State gazette volume 84 from 21.10.2022

To participate in the competition Metodi Traykov presents 1 habilitation thesis and 7 titles of scientific articles, which do not repeat the articles submitted for occupying the academic position "Chief Assistant", and Educational and Scientific Degree "Doctor". The reference contains summaries of the scientific articles, submitted for the competition.

CONTENTS

GROUP C, INDICATOR 3 (MONOGRAPH)

1. **Traykov, M. G. The Protein Folding Problem – approaches, models and algorithms, Publishing "Education and knowledge", Sofia, 2022, ISBN 978-619-7515-28-2, 208 pages**

Summary: The monographic work with the title "The Protein Folding Problem – approaches, models and algorithms" presents the results of interdisciplinary research in the field of Bioinformatics, related to molecular biology, physical chemistry, computational chemistry, important sections of physics, bioinformatics, biology, and mathematics. The focus of the monograph is on the fundamental question of the mechanism and powers that form the tertiary structure of the proteins. The tertiary structure of proteins determines the biological properties of the proteins. In other words, the monograph is devoted to the topic of predicting the tertiary structure of proteins based on their primary structure. This problem is one of the main research problems in structural bioinformatics. The solution to this problem will have a great impact on unraveling the functions of a given protein, which are more closely related to the tertiary structure of proteins than to their primary structure. Any progress in this field is highly valued by researchers because it contributes to a better understanding of the principles of the functioning of living matter.

The monograph presents models, algorithms, approaches, and techniques for predicting the tertiary (3D) structure of proteins. Two points of view on the problem are considered – biologists' point of view, which are based on the biological characteristics of proteins, and mathematicians' and programmers' points of view, which are based on integer optimization techniques, as well as algorithms for solving optimization problems, in order to use modern software such as CPLEX and GUROBI.

The monographic work with the title "The Protein Folding Problem – approaches, models and algorithms" represents a comprehensive and thorough study in the field of Bioinformatics. It has complex, interdisciplinary nature and contains scientific and scientific-applied contributions.

Computational experiments show that the idea of dividing the problem into sub-problems works well for long protein sequences. The comparisons of obtained results with results obtained by known in the literature algorithms, solving the problem shown that the developed models and algorithms are qualitative and reliable

GROUP D, INDICATOR 7. SCIENTIFIC ARTICLES IN JOURNALS THAT ARE REFERENCED AND INDEXED IN WORLD-RENOWNED DATABASES OF SCIENTIFIC INFORMATION, SUCH AS SCOPUS AND WEB OF SCIENCE.

1. **T.Z. Todorova, M.G. Traykov, A.V. Tadjer, Zh.A. Velkov, 2013. Structure of flavones and flavonols. part I: role of substituents on the planarity of the system. Computational and Theoretical Chemistry, vol. 1017, pp. 85-90. (Impact Factor: 1.403, Web of science: Q4)**

Summary: The article represents the first part of extensive research on the effect of -OH, -NH_2, -NO_2 and other substituents on the planarity (and the level of delocalization) of a series of flavones and flavonols. This feature is particularly important in terms of the biological activity of flavonoids. The values of the dihedral angles were obtained from the optimized in gas phase and in water geometries at the density functional theory B3LYP/6-31G(d,p) level.

In last years, flavonoids have attracted a generous interest because they are powerful radical scavengers. Kinetics analyses of the protein tyrosine kinases inhibition show that flavonoids are competitive inhibitors of the nucleotide adenosine triphosphate. There is substantial evidence indicating that the inappropriate or enhanced expression of these enzymes may also contribute to the transformed state of cells in many human malignancies. Some flavones such as primuletin, chrysin, and luteolin show vasorelaxing, antioxidative, and chemopreventive effects, respectively. A number of studies show that flavonoids manifest anti-inflammatory action via their ability to modulate free radical production by phagocytic leukocytes. Flavonoids have been identified as good inhibitors of the aldose reductase, an enzyme of the polyol pathway which regulates glucose blood levels in the body and has been linked with numerous detrimental complications.

Various factors influence the angle between the two rings of the flavonoids and thus the degree of delocalization therein. On the one hand, there exists a tendency to stabilization of the molecule by extending the conjugated system and the transfer of electron density to the carbonyl group at position 4 in ring C. On the other hand, there is repulsion or attraction between substituents at positions 3 and 20.

If there is a hydrogen at position 3, it repels the hydrogen at position 20 and only an electron-releasing functional group (NH2 or OH) at 40 can decrease this angle. The same functional groups at 30 do not have an appreciable effect on the dihedral angle between the two rings; so do the functional groups with electron-withdrawing effect.

2. **Traykov, M., Mavrevski, R., Angelov, S., Trenchev, I. (2022). Bioinformatics: Model Selection and Scientific Visualization. In: Zlateva, T., Goleva, R. (eds) 18th EAI International Conference on Computer Science and Education in Computer Science, CSECS 2022, Virtual, Online, 24 June 2022-27 June 2022. Lecture Notes of the Institute for Computer Sciences, Social-Informatics and Telecommunications Engineering (LNICST), vol 450. Springer, Cham, pp. 92-101. https://doi.org/10.1007/978-3-031-17292-2_8 (Scopus, SJR)**

Summary: The paper summarizes and shows the basic criteria for model selection in bioinformatics to develop a reliable approach for predicting different relationships in bioinformatics. In addition, the article describes briefly the application of computer modeling in the analysis of results obtained by mathematical models for problems in bioinformatics, such as protein folding problems, which is an analysis of biological structures and an example for application of a model selection criteria to select a model for solving a problem in bioinformatics.

3. **Yanev N., Traykov M., Milanov P., Yurukov B., 2018. A new classifier for protein fold class recognition. C. R. Acad. Bulg. Sci., vol. 71(7), pp. 885-892. (Impact Factor: 0.27, Scopus: SJR(0.205))**

Summary: The article contains a description of a new multi-group classifier with better true positive results for proteins' fold classification. The time complexity of the classifier allows obtaining results for a huge dimension (8000) of the feature space in an affordable time.The determination of the convex hulls is obtained as a heuristic solution to problems of classification and pattern recognition in computational geometry. The obtained results are compared with already published results on 27-class protein fold classification problems. The results are quite promising both in the correctness of classifications and in the time for making them. The time complexity of the classifier allows for filling the gap for huge dimensions (400 and 8000) of the feature space in affordable time.

4. **Trenchev I., Traykov, M., Mavrevski, R., Popchev, V., 2018. Investigation of the relationship between the hydrophobicity of an amino acid and codon, which shall encodes. WSEAS Transactions on Systems and Control, vol. 13, pp. 401-408, E-ISSN: 2224-2856. (Scopus: SJR(0.157))**

Summary: This article is a brief review of mathematical models for studying the genetic code. It contains a study on how the hydrophilicity of amino acids affects protein structure. The

presented model describes nucleotide sequences at different levels of protein evolution. Also, the article contains a mathematical analysis of the construction and possible evolutionary scenario. The evolution of the code is based on formal schemes whose relevance is a simple mutation and cardinality of a synonymous set that codes one amino acid.

The notion of optimality of the modern genetic code may have different contexts in biology, biochemistry and molecular mechanics, mathematics, and bioinformatics. As it is seen from the perspective of the evolutionary development of species optimum is a code that is not resistant to mutations. From a mathematical point of view, the minimum number of mutations, i.e. the error, means minimizing the effects of errors, which is an optimization problem. Optimality criteria for further complicate the problem because they are different, (such as the length of the codons, the number of nucleotides, the number of codons in the synonym set, the position of the mutation in codons, and others) and because their combination is a part of modeling.

5. **Mavrevski, R., Traykov, M., Trenchev, I., Trencheva, M., 2018. Approaches to modeling of biological experimental data with GraphPad Prism software. WSEAS Transactions on Systems and Control, vol. 13, pp. 242-247, E-ISSN: 2224-2856. (Scopus: SJR(0.157))**

Summary: The main contribution of this article is the step-by-step description of the application of non-linear regression analysis for fast and efficient data analysis in biology. To achieve this aim is used non-linear regression analysis method by GraphPad Prism software. Also, the article contains a description of the modeling of specific experimental data taken from the literature. Non-linear regression is an extremely useful tool in analyzing data, but choosing a model is a scientific decision based on biology, chemistry or physiology, etc., and not be based solely on the shape of the graph.

The purpose of non-linear regression analysis is to fit a model to the data. Non-linear regression is one of the most powerful and useful features in Prism. Using it, each model can be compared to our data to plot a curve and determine the best-fitting values for the model parameters. The Prism software can compare models and answer the question " For each data set, which of two equations (models) fits best?". The answer to this question can be essential for the biological sciences because there we may use mathematical models to simulate biological processes. To understand complex biological systems such as cells, tissues, or others, it is not enough to identify and characterize the individual molecules in the system. It is necessary, also, to gain a thorough

understanding of the interaction between molecules and different pathways. Computational models help scientists to analyze systems and develop hypotheses to guide the design of new experimental tests.

6. **Mavrevski, R., Traykov, M., 2019. Visualization software for Hydrophobic-Polar protein folding model. Scientific Visualization, vol. 11(1), pp. 11-19, (Scopus: SJR(0.268))**

Summary: The paper presents software for the visualization of results obtained by algorithms to solve the protein folding problem in 2D HP lattice models. The simplest and most used model for the protein folding problem is the Hydrophobic-Polar (HP) model. The HP model denotes the amino acids as Hydrophilic (H) or Polar/Hydrophilic (P). The folding of a protein's amino acids sequence can be represented as self-avoiding walks in a 2D or 3D lattice, where the optimal conformation has a maximum number of contacts between H amino acids (H-H contacts) that are not adjacent in the amino acid sequence. The input of the program is an HP sequence and results, generated by a protein folding model, implemented and solved by optimization software such as CPLEX or GUROBI. This visualization software is a valuable tool for studying protein folding in the HP model. It can be a great pedagogical tool to help students to gain additional bioinformatics skills as well as learn more about proteins and processes associated with them, such as the protein folding process.

7. **Mavrevski, R., Traykov, M., Trenchev, 2019. Finding the shortest path in a graph and its visualization using C# and WPF. International Journal of Electrical and Computer Engineering (IJECE), vol. 10(2), pp. 2054-2059. (Scopus: SJR(0.322))**

Summary: This paper is a study of a well-known technique for finding the shortest path, using the C# programming language and modern technologies such as WPF, that can be used for finding new ideas for solving more complex problems and refining algorithms suitable for use in a programming competition. The article describes software for solving the shortest path problem. As is known, this problem is a classic problem in mathematics and computer science with applications, for example, in economics (sequential decision-making, social network analysis, etc.) and other areas. That work is an example of the implementation and application of Dijkstra's algorithm for finding the shortest path between two vertices in a connected, undirected graph, which often can be encountered as a part of more complex tasks for programming contests.

28.02.2023 Signature:……..

/ Metodi Traykov /